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| 10/563,498 | 06/07/2006 | Siegfried Ansorge | 013183.00055 | 1382 |

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| EXAMINER | |
|---|---|
| HA, JULIE | |

| ART UNIT | PAPER NUMBER |
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| 1654 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,498 | ANSORGE ET AL. | |
| | Examiner | Art Unit | |
| | JULIE HA | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *January 29, 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-13,15-22 and 24-31* is/are pending in the application.

4a) Of the above claim(s) *1-4,6-12,15-21,23 and 26-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,13,22,24-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Amendment after Non-final rejection filed on January 29, 2010 is acknowledged. Claim 23 has been cancelled and new claims 25-31 have been added. Claims 1-13, 15-22 and 24-31 are pending in this application. Applicant elected Group II and species (Lys[$ZNO_2$])thiazolidide) as DP IV inhibitor, actinonin as the APN inhibitor, benign fibrotic and sclerotic diseases as the species of diseases, oral as the systemic application, and creams as the topical application in the reply filed on January 17, 2008. Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election was treated as an election without traverse. The restriction requirement was deemed proper and made FINAL in the previous office action. Claims 1-4, 6-12, 15-21, 23 and 26-31 are/remain withdrawn from further consideration, as being drawn to nonelected inventions and species. Claims 5, 13, 22 and 24-25 are examined on the merits in this office action.

***Withdrawn Rejection***

2. Objection to claim 5 is hereby withdrawn in view of Applicant's amendment to the claim.

3. Objection to the abstract is hereby withdrawn in view of Applicant's amendment to the abstract.

4. Rejection to claims 5 and 22 under 35 U.S.C. 112, second paragraph, as being indefinite, is hereby withdrawn in view of Applicant's amendment to the claims.

***Maintained and Revised Rejection***

***35 U.S.C. 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 5, 13, 22 and 24-25 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Ansorge (WO 02/053170 (published July 11, 2002), machine translation used) as evidenced by Andriessen et al (Journal of Pathology, 1998, 186: 192-200) or Machesney et al (American Journal of Pathology, 1998, 152(5): 1133-1141) or Castagnoli et al (Clin. Exp. Immunol., 1990, 82: 350-354).

The instant claim is drawn to a method utilizing the inhibitor combinations (DPIV inhibitor and APN inhibitor) for treatment of benign fibrotic and sclerotic diseases, wherein therapy comprises an inhibition of activation, DNA synthesis and proliferation of human fibroblasts.

Ansorge et al teach the combined used of DP IV inhibitor (Lys[Z($NO_2$)]thiazolidide) and APN inhibitor (actinonin) for the treatment of atherosclerosis and dermatological diseases (see paragraph 5 of the translated document). Furthermore, the reference teaches simultaneous administration of inhibitors and the administration is as topical application in the fore of creams, ointments, pastes, gels, solutions, spray, liposomes and systemic application to the oral, transdermal, intravenous, subcutaneous, intracutaneous, intramuscular with

pharmaceutically acceptable carrier (see paragraphs 6 and 9 of the translated document). Since the elected compound is taught by the reference and is disclosed that the compound can be used to treat dermatological diseases. The reference teaches the treatment of atherosclerosis, which is a species of sclerosis. The reference teaches the combination therapy utilizing DP IV inhibitor and APN inhibitor to treat dermatological illnesses by inhibition of DNA synthesis, meeting the limitation of claims 5, 13, 22 and 24-25. Therefore, since Ansorge reference teaches the use of DP IV inhibitor (Lys[Z($NO_2$)]thiazolidide) and APN inhibitor (actinonin) to treat atherosclerosis and dermatological diseases (associated with hyperproliferation of keratinocytes), this administration would treat other benign fibrotic and sclerotic diseases. Andriessen et al teach that hypertrophic scarring revealed an increase in basal keratinoctye proliferation rate (see abstract and Discussion), indicating that keratinocytes are involved in hypertrophic scarring. Furthermore, Machesney et al teach that keratinocytes play roles in hypertrophic scar epidermis (see abstract and Discussion). Castagnoli et al further teaches that sections from all hypertrophic scars showed an anomalous expression of HLA-DR molecules on keratinocytes and fibroblasts, further showing evidence that both keratinoctyes and fibroblasts are involved in hypertrophic scars (benign fibrotic and sclerotic diseases). Therefore, the reference meets the limitations of claims 5, 13, 22 and 24-25.

***Response to Applicant's Arguments***

7. Applicant argues that "the present claims are distinct from the reference of Ansorge because, the claims specify that the inhibitors are administered to an individual in need of the recited therapy and there is no such individual described in Ansorge." Applicant further argues that "Ansorge does not anywhere disclose administering the recited combination to an individual who is in need of therapy for hyperproliferation of fibroblasts, which is required, for example, by present claim 13, and where the limitation is not present in a "wherein" clause." Applicant argues that "the "wherein" clause in the present claims do in fact limit the claims to particular structural features. The wherein clauses specify effects of practicing the method…specify the patient population on which the method is practiced." Applicant further argues that "whether the methods disclosed in Ansorge "would treat" other diseases is immaterial to the salient question of whether the reference of Ansorge does in fact expressly or inherently disclose such a treatment." Applicant further argues that there is no evidence in Castagnoli et al or elsewhere on the record that expression of HLA-DR molecules on fibroblasts signifies that the fibroblasts are hyperproliferating in association with a dermatological diseases."

8. Applicant's arguments have been fully considered but have not been found persuasive. Ansorge reference teaches all of the active methods of the instant claims. Ansorge et al teach the combined used of DP IV inhibitor (Lys[Z($NO_2$)]thiazolidide) and APN inhibitor (actinonin) for the treatment of atherosclerosis and dermatological diseases associated with hyperproliferation of keratinocytes. The reference teaches that the administration of the combination therapy inhibits DNA synthesis. Furthermore,

atherosclerosis is a type of sclerotic diseases. Instant claim 5 does not define a patient population. A person suffering from atherosclerosis would be in need of treatment for benign fibrotic and sclerotic diseases. In light of definition provided in the instant specification, sclerotic diseases include atherosclerosis. For example, the instant specification provides examples of sclerotic diseases (see paragraph [0017] instant specification US 2007/0042938) and the definition is not closed. Different diseases are encompassed within the definition of sclerotic diseases. Therefore, the treatment of atherosclerosis and other dermatological diseases disclosed in the reference meets the limitation of instant claim 5. In regards to Applicant's argument that "Ansorge does not anywhere disclose administering the recited combination to an individual who is in need of therapy for hyperproliferation of fibroblasts, which is required, for example, by present claim 13, and where the limitation is not present in a "wherein" clause." Instant claim 13 recites, "a method for therapy of dermatological diseases including a hyperproliferation and changed differentiation states of fibroblasts." Claim 13 encompasses more than just hyperproliferation and changed differentiation states of fibroblasts. It encompasses all other dermatological diseases, which is disclosed in the Ansorge reference.

Furthermore, although Table 1 of Ansorge reference is not identical with the diseases treated by instant application, there is sufficient evidence that both keratinocyte and fibroblasts are involved in the diseases disclosed by Table 1 of Ansorge reference instant claims. In other words, there is sufficient evidence of similarity which is deemed to be present between the instantly claimed invention of claims 5, 13, 22 and 24-25 and the WO 02/053170 (or equivalence '969). For further

support, see the references of record (Andriessen et al or Machesney et al or Castagnoli et al). Andriessen et al teach that hypertrophic scarring revealed an **increase in basal keratinoctye proliferation rate** (see abstract and Discussion), indicating that keratinocytes are involved in hypertrophic scarring. Furthermore, Machesney et al teach that **keratinocytes play roles in hypertrophic scar** epidermis (see abstract and Discussion). Castagnoli et al further teaches that sections from all hypertrophic scars showed an anomalous **expression of HLA-DR molecules on keratinocytes and fibroblasts**, further showing evidence that both keratinoctyes and fibroblasts are involved in hypertrophic scars (benign fibrotic and sclerotic diseases). These references clearly discloses that keratinocyte and fibroblasts are involved in benign fibrotic and sclerotic diseases (post-infectious and post-traumatic, hypertrophic scars, keloids). Hypertrophic scars and keloids, for example, are diseases characterized by both proliferation of keratinocytes and fibroblasts, and as such, using the same compound (i.e., compounds claimed and disclosed in WO 02/053170 or '969, as Applicant pointed out), would inherently must treat benign fibrotic and sclerotic diseases, because it is the same population being treated (i.e., patients having disease pattern and/or condition associated with hypertrophic scars and keloids) in both situations.

Therefore, in the absence of evidence to the contrary or specific structural limitations, the prior art teachings clearly discloses the use of the claimed compounds to treat dermatological disease conditions of benign fibrotic and sclerotic diseases which include hypertrophic scars and keloids in a patient as well as to inhibit the activation of

DNA synthesis of proliferation of human fibroblasts, and as such anticipates claims 5, 13, 22 and 24-25.

With respect to "wherein the therapy comprises an inhibition of activation, DNA synthesis and proliferation of human fibroblasts" according to MPEP 2111.04: "Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

(A) "adapted to" or "adapted for" clauses;

(B) "wherein" clauses; and

(C) "whereby" clauses.

The determination of whether each of these clauses is a limitation in a claim depends on the specific facts of the case. In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a "whereby' clause states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention." Id. However, the court noted (quoting Minton v. Nat'l Ass'n of Securities Dealers, Inc., 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited." Id. <". In the instant case, it is not deemed that the "wherein" clause limits the claim to particular structural features. As Applicant indicated, "the wherein clause specify effects of practicing the method…specify the patient population on which the method is practiced",

the wherein clause only recite the "effect" of the therapy. The inhibition of activation, DNA synthesis and proliferation of human fibroblast would necessarily occur, because all of the structural limitations are disclosed by the Ansorge reference. That is, the same active method steps, same type of compound is being administered to the same patient. Therefore, the end effect would occur. The MPEP states the following: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Altas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51, USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

***Conclusion***

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claim is allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654